

Seminario
Angiogenesi tumorale

<http://www.biooncology.com/research-education/vegf/images/Angiogenesis-tumor-growth.jpg>



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OBITUARY

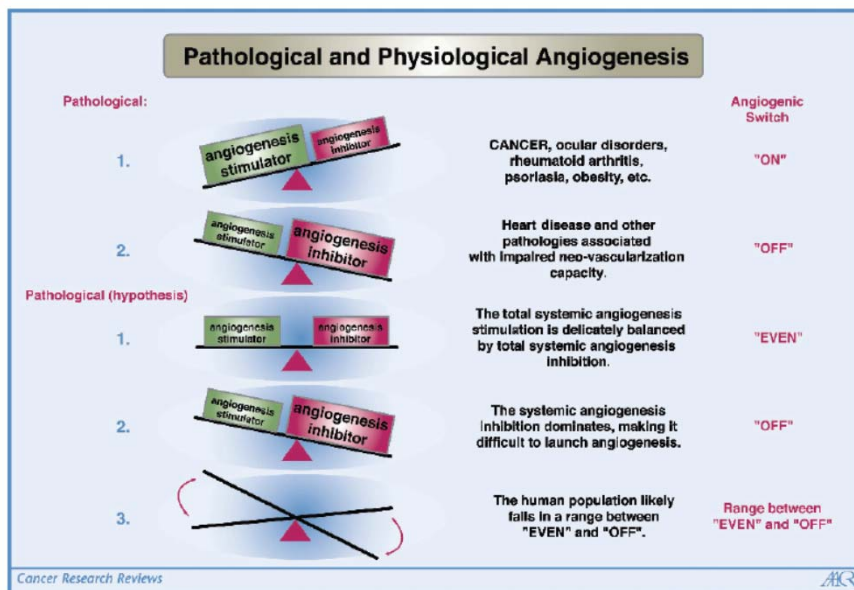
M. Judah Folkman (1933-2008)

Scientist, surgeon and creator of the field of angiogenesis research.

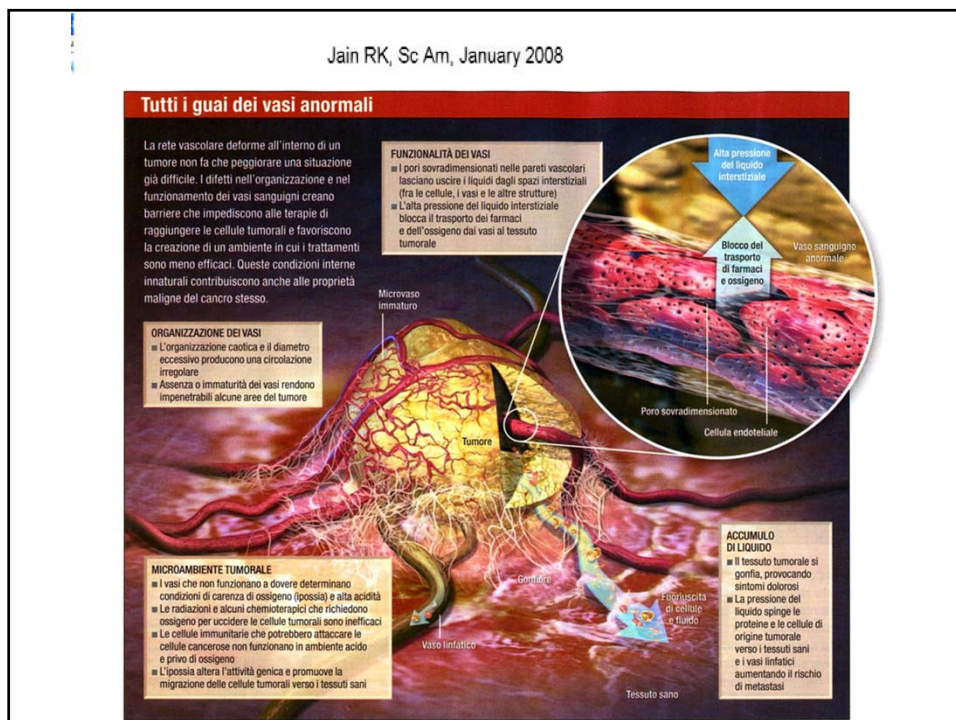
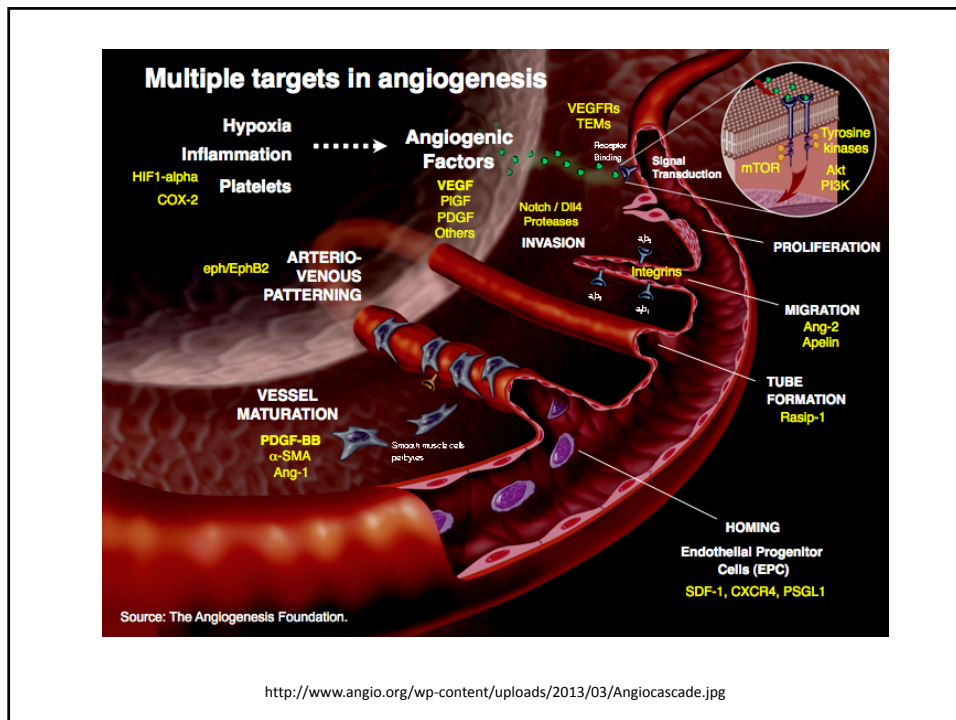


Che cosa è l'angiogenesi?

- **Angiogenesi:** reclutamento di cellule endoteliali a partire di vasi pre-esistenti.
- **Vasculogenesi:** attivazione di precursori endoteliali

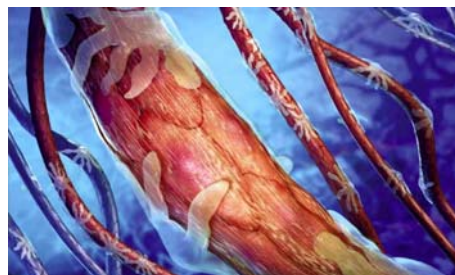
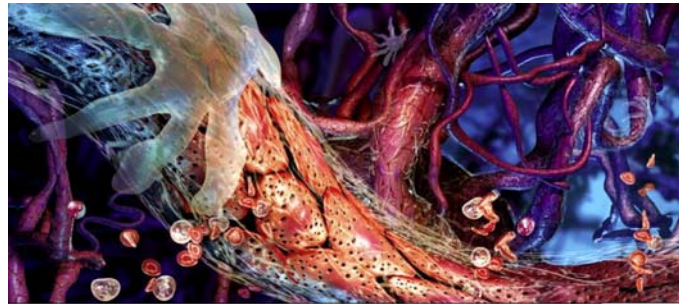
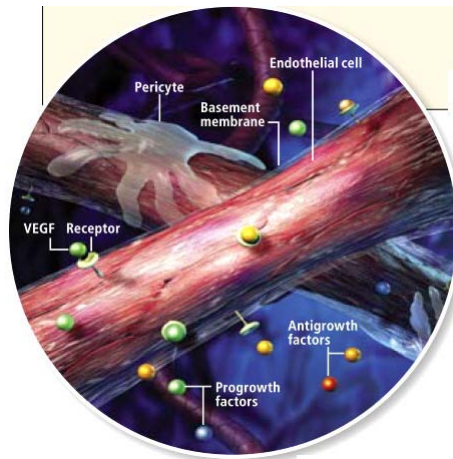


Nyberg P, Xie L, Kalluri R. **Endogenous inhibitors of angiogenesis.** Cancer Res. 2005 May 15;65(10):3967-79.



▼ CRESCITA E MANTENIMENTO DEI VASI SANI

Le cellule endoteliali formano vasi sanguigni in risposta ai segnali di molecole che stimolano e inibiscono la crescita. I vasi sono sostenuti dai periciti e dalla membrana basale.



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The Angiogenic Process

Endothelial cell activation and survival (eg. VEGF, bFGF)

Basement membrane degradation (eg. MMPs, uPAR)

Endothelial cell proliferation and migration (eg. VEGF, bFGF)

Tube formation, elongation, and remodeling (eg. Integrins)

Maturation (pericytes associated with vasculature)

Intravascular modulators of angiogenesis

Griffioen and Melema. *Pharmacol Rev.* 2000;62:237.

http://www.medscape.org/viewarticle/548836_3

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Normal and Tumor Vasculature

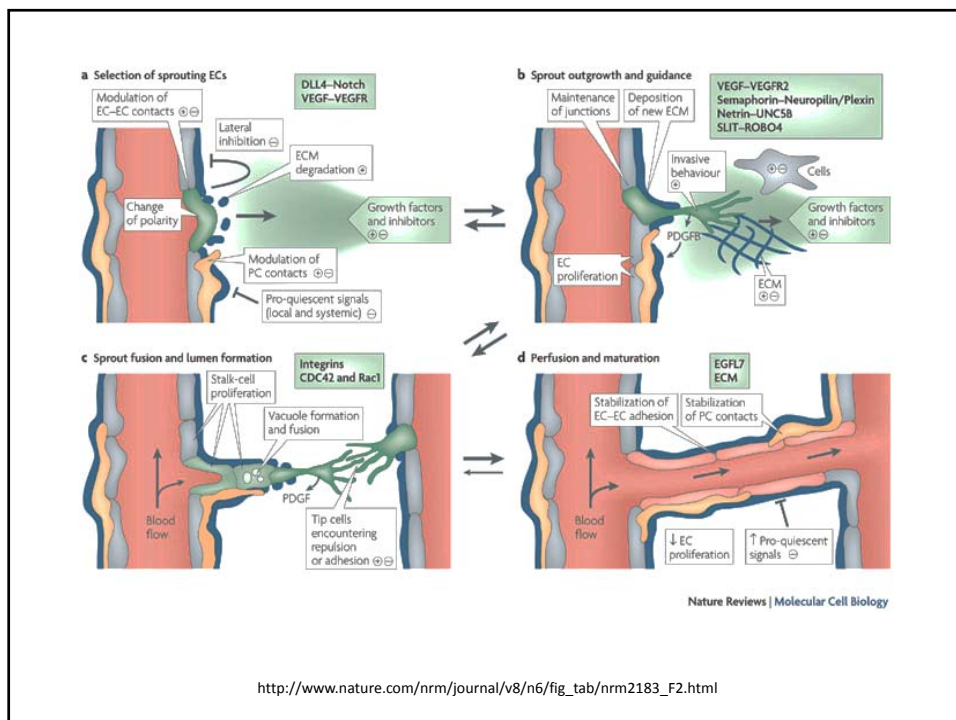
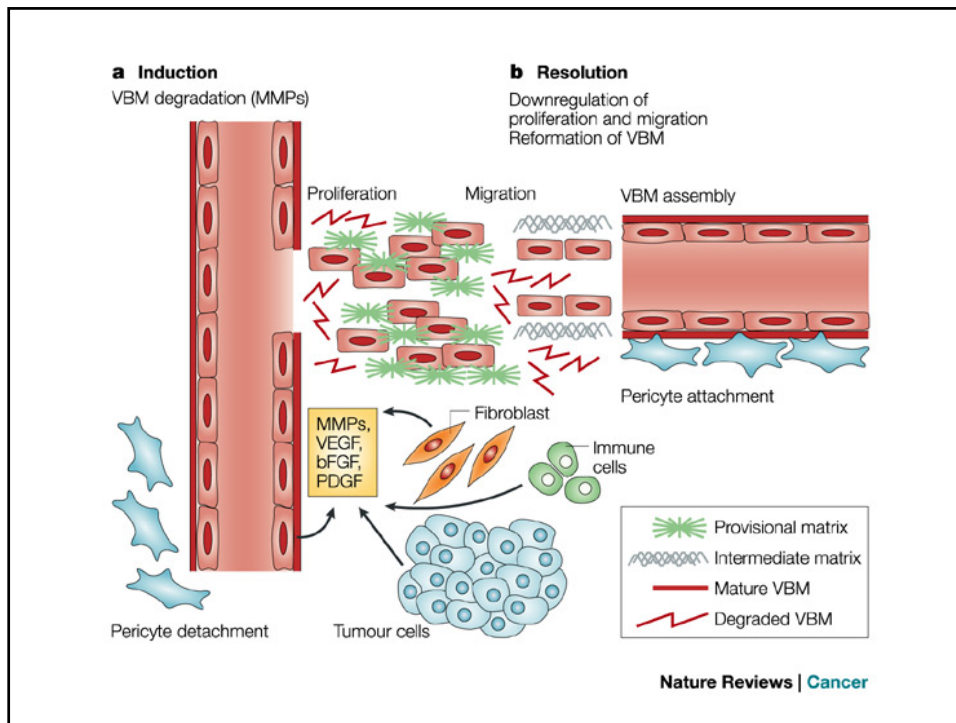
Normal Blood Vessels	Tumor Blood Vessels
Maturation factors present (eg. Ang-1) ¹	Growth and survival factors (eg. VEGF, bFGF) present ²
Less dependent on cell survival factors ²	Leaky ³
Less permeable ³	Fewer supporting cells ²
Supporting cells present ²	Preferential expression of $\alpha_3\beta_1$, $\alpha_5\beta_1$, and $\alpha_v\beta_3$ integrins ¹
Reduced Integrin expression ¹	

Properties of Tumor Vasculature

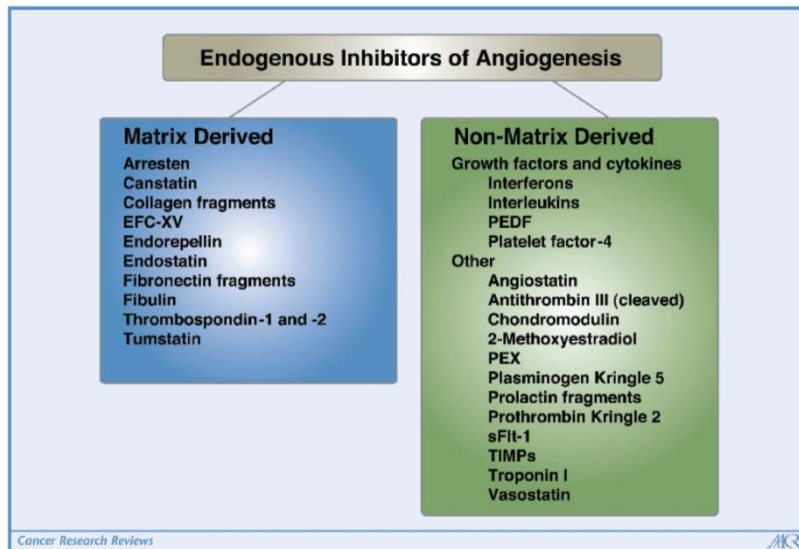
- Tortuous, dilated, poorly organized
- Perivascular cells abnormal
- Hyperpermeable
 - Results in increased interstitial pressure
 - Decrease in diffusion of drugs into the tumor

1. Griffioen. *Pharmacol Rev.* 2000;62:237
 2. Blou and Sarfi. *Nat Med.* 2001;7:532. Adapted with permission from MacMillan Publishers
 3. Jain. *Nat Med.* 2001;7:987. Adapted with permission from MacMillan Publishers

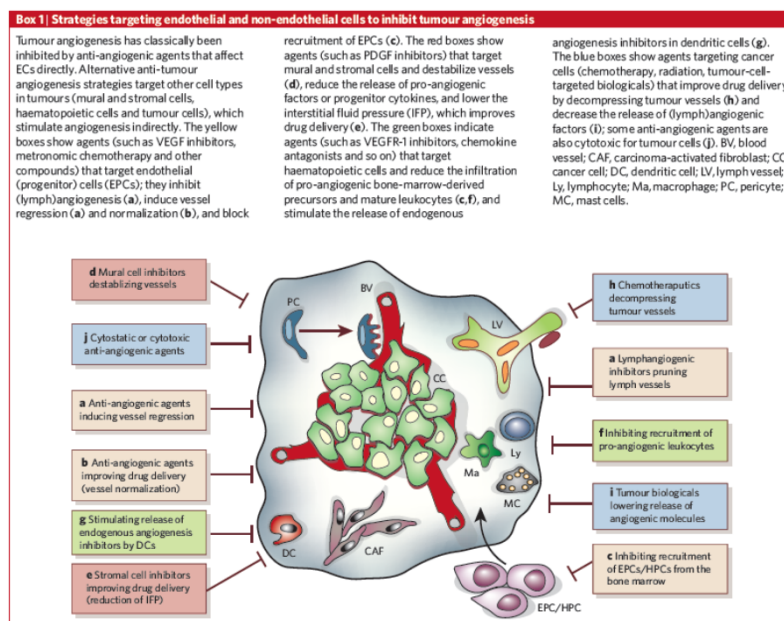
http://www.medscape.org/viewarticle/548836_3



http://www.nature.com/nrm/journal/v8/n6/fig_tab/nrm2183_F2.html



Nyberg P, Xie L, Kalluri R. **Endogenous inhibitors of angiogenesis.** *Cancer Res.* 2005 May 15;65(10):3967-79.



Carmeliet P. **Angiogenesis in life, disease and medicine.** *Nature.* 2005 Dec 15;438(7070):932-6.